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GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN,
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ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
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GN, GQ, GW, ML, MR, NE, SN, TD, TG).

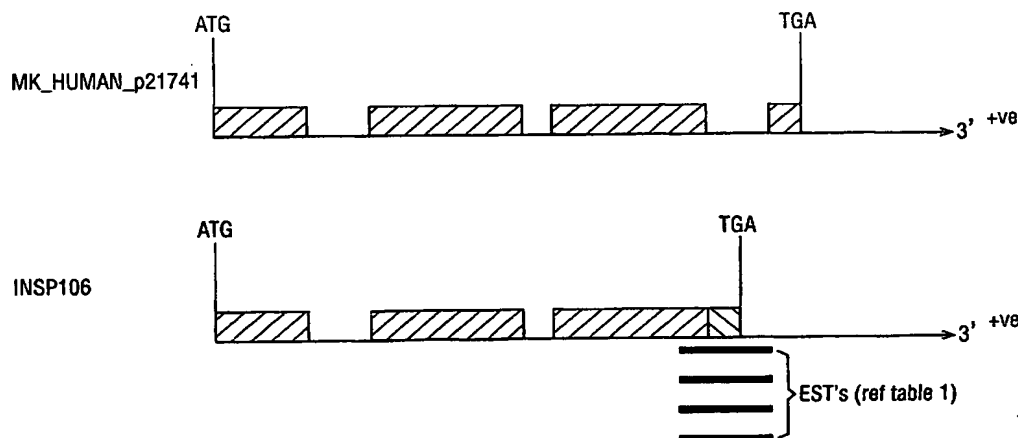
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For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: MIDKINE-LIKE PROTEIN



(57) Abstract: The invention is based on the discovery that the INSP106 protein is a novel splice variant of a known midkine family member (swallIP21741MK_HUMAN).

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 03/05374

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/71 C12N15/12 C12N5/10 C12Q1/68 G01N33/53
A61K38/18 A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N C12Q A61K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, EMBL, GENSEQ, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE UNIPROT 'Online! 1 October 2000 (2000-10-01) IKEDA, S. ET AL.: "Midkine precursor" Database accession no. Q9NOE6 XP002282467	1, 2, 4-45
X	EP 0 476 233 A (AMERICAN CYANAMID CO) 25 March 1992 (1992-03-25) claims 1-13	4, 7-15, 19-45
X	US 6 083 907 A (MURAMATSU TAKASHI ET AL) 4 July 2000 (2000-07-04) SEQ ID NO:2 and SEQ ID NO:3 column 4, line 10 -column 8, line 18 -/-	4, 7-15, 19-45

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- *Z* document member of the same patent family

Date of the actual completion of the international search

27 May 2004

Date of mailing of the international search report

14/06/2004

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INTERNATIONAL SEARCH REPORT

In **International Application No**
PCT/GB 03/05374

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 01/36635 A (BURGESS CATHERINE ;PRAYAGA SUDHIRDAS K (US); CURAGEN CORP (US); MA) 25 May 2001 (2001-05-25) page 3, last paragraph -page 8, paragraph 3 page 48, paragraph 2 -page 49, paragraph 1 page 50, paragraph 2 -page 83, paragraph 2 page 84, paragraph 1 -page 111, paragraph 2</p>	4,7-15, 19-45
A	<p>AKHTER SHAMIMA ET AL: "Clusters of basic amino acids in midkine: Roles in neurite-promoting activity and plasminogen activator-enhancing activity" JOURNAL OF BIOCHEMISTRY (TOKYO), vol. 123, no. 6, June 1998 (1998-06), pages 1127-1136, XP001189525 ISSN: 0021-924X cited in the application</p>	
A	<p>BERNARD-PIERROT ISABELLE ET AL: "Dominant negative effectors of heparin affinity regulatory peptide (HARP) angiogenic and transforming activities" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 277, no. 35, 30 August 2002 (2002-08-30), pages 32071-32077, XP002245580 ISSN: 0021-9258 cited in the application</p>	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 03/05374

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 35-37 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 16-18 (complete) and 14, 19, 31, 33-37 (partially)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 16-18 (complete) and 14, 19, 31, 33-37 (partially)

Present claim 14, 19, 31, 33-37 relate to a ligand and uses thereof which is defined by reference to a desirable characteristic or property, namely, that binds specifically to a polypeptide according to any one of claims 1-7. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those of the claims as far as they relate to the ligands which are supported and disclosed, i.e the antibodies specific for the polypeptide of claims 1-7 (e.g claim 15).

Present claims 16-19, 31, 33-37 relate to a compound and uses thereof which is defined by reference to a desirable characteristic or property, namely, that either increases, decreases the level of expression or activity of the polypeptides according to claims 1-7. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has not been carried out for those of the claims as far as they relate to the unidentified compound.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

In International Application No

PCT/GB 03/05374

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